REMARKS/ARGUMENTS

Claims 1 to 30, as amended, are pending. Applicant has amended claims 1 to 6, 10, 11, 16 to 21, 23, 24, 28 and 29. The amendments find full support in the original specification and claims. No new matter is presented. In view of the above amendments and following remarks, Applicant respectfully requests favorable reconsideration and a timely indication of allowance.

The Examiner objected to the abstract, specification and claims for containing file locators and headers containing Applicant's representative's reference numbers. Applicant respectfully submits that such file locators and headers are acceptable in patent applications. The undersigned's firm has submitted thousands of applications containing such information, and the Patent Office has not objected to the inclusion of such information or had any difficulty printing the issued patents. If the Examiner continues to maintain this objection, Applicant respectfully requests that he provide a rule or M.P.E.P. provision that prohibits the inclusion of such information in the application.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 1 to 30 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. First, the Examiner contends that claims 1 and 18 to 21 are indefinite for reciting the step of providing, which allegedly does not represent a positive active method step. Although Applicant respectfully disagrees, in an effort to advance prosecution, Applicant has amended the claims to remove the step of providing, thereby obviating this ground of the rejection.

The Examiner objected to the recitation of "lyophilized blood protein/hydroxypropyl-α-cyclodextrin" and "lyophilized fibrinogen/hydroxypropyl-α-cyclodextrin" in claims 18, 19 and 21. Specifically, the Examiner states that these

claims contain the use of an alternative expression wherein the limitation covers two elements. Applicant has amended claims 18, 19 and 21, as well as several other claims containing the objected-to expression, in an attempt to obviate this ground of the rejection. If Applicant's amendments do not obviate the rejection, Applicant respectfully requests clarification or a suggested amendment so that Applicant can better address the Examiner's concern.

The Examiner contends that claims 3 to 6 are indefinite for reciting "at least about." Although Applicant respectfully disagrees, in an effort to advance prosecution, Applicant has amended these claims to obviate this ground of the rejection.

Additionally, the Examiner contends that claims 26 and 28 to 30 are redundant of claims 22 to 25. Applicant respectfully disagrees. As acknowledged by the Examiner, claim 22 recites a lyophilized solution whereas claim 26 recites a stabilized blood protein solution, but the Examiner states that both solutions have the same components and therefore there would appear to be no difference in scope. However, claim 26, by not requiring that the solution be lyophilized, is broader, at least in that respect, than claim 22. As a result, claims 22 and 26 are not duplicative.

For all these reasons, Applicant respectfully requests that the rejection under section 112, second paragraph, be withdrawn.

Rejection Under 35 U.S.C. § 103

The Examiner rejected claims 1 to 30 under 35 U.S.C. § 103(a) as allegedly unpatentable over Neurath et al. (U.S. Patent No. 4,540,573) taken with Fredholt et al. (Int'l. J. Pharm.) or Fukunaga et al. (U.S. Patent No. 5,482,929). Applicant respectfully traverses this rejection.

Claim 1 recites a process for enhancing the solubility of a blood protein solution comprising: (a) adding to a blood protein solution hydroxypropyl-α-cyclodextrin in an amount sufficient to form a stable complex with the protein; and (b) lyophilizing the solution of step (a) to form a lyophilized complex of the protein and hydroxypropyl-α-cyclodextrin. Such a method is not taught by the cited references, even in combination.

Neurath is directed to a method of inactiviting viruses in blood proteins comprising contacting the protein with a dialkylophosphate or trialkylphosphate. Neurath states that the process can be combined with other methods of inactivating viruses, such as by heating the protein in the presence of a stabilizer. The Examiner acknowledges that Neurath does not teach or suggest that the stabilizer can be hydroxypropyl-α-cyclodextrin. Moreover, Neurath does not teach or suggest that the "stabilizer" can also be used to enhance the solubility of the protein. In fact, Neurath nowhere addresses the potential solubility problem, much less suggests a solution to the problem.

To remedy the deficiencies of Neurath, the Examiner relies on Fredholt and Fukunaga. Fredholt is directed to stabilizing desmopressin against α-chymotrypsin-catalyzed degradation using hydroxypropyl cyclodextrins (α, β and γ). Fredholt states at page 224, column 2, that "[c]yclodextrins are known to form inclusion complexes with a variety of chemical substances enabling enhanced solubility, protection against enzymatic degradation and absorption enhancement." Nothing in Fredholt teaches or suggests using cyclodextrins to stabilize <u>blood proteins</u>, much less using hydroxypropyl-α-cyclodextrin to do so.

Moreover, there is no motivation to combine Fredholt with Neurath, as Neurath addresses protein stabilization during heat treatment and Fredholt is directed to stablizing desmopressin, not a blood protein, against enzyme-catalyzed degradation. These are two very different problems, and one skilled in the art

looking to solve one of these problems would not look to the other problem for a common solution.

Fukanaga et al. is directed to a composition of stabilized FGF that contains an aluminum salt of cyclodextrin sulfate. First, Fukanaga does not teach or suggest using hydroxypropyl-α-cyclodextrin. Instead, Fukanaga is using an aluminum salt of, *inter alia*, hydroxypropyl-α-cyclodextrin sulfate. Fukanaga provides no motivation to replace the aluminum salt of cyclodextrin sulfate with a cyclodextrin, as Fukanaga emphasizes the importance of using the aluminum salt. (See column 2, lines 19 to 31.) In fact, replacing the aluminum salt of cyclodextrin sulfate with a cyclodextrin would defeat the intended purpose of Fukanaga, which is impermissible for establishing a *prima facie* case of obviousness. See M.P.E.P. § 2143.01. For this reason alone, Fukanaga does not remedy the deficiencies of Neurath.

Moreover, Fukanaga is directed to stabilizing FGF, for example, in the presence of heat. Fukanaga, like Neurath, does not teach or suggest that the aluminum salt of cyclodextrin sulfate, much less hydroxypropyl-α-cyclodextrin, can be used to enhance the solubility of the FGF. For this reason as well, Fukanaga does not remedy the deficiences of Neurath.

For all these reasons, the cited references, even in combination, do not render obvious the claimed invention. Applicant therefore respectfully requests that the rejection under section 103 be withdrawn.

In view of the foregoing amendments and remarks, Applicant respectfully submits that pending claims 1 to 30 are in condition for allowance, and a timely indication of allowance is respectfully requested. If there are any remaining issues that can be addressed by telephone, Applicant invites the Examiner to contact the undersigned at the number indicated below.

Respectfully submitted,

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